

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/013327

International filing date: 19 April 2005 (19.04.2005)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/620,999
Filing date: 21 October 2004 (21.10.2004)

Date of receipt at the International Bureau: 30 May 2005 (30.05.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

1321301



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

May 17, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: 60/620,999

FILING DATE: October 21, 2004

RELATED PCT APPLICATION NUMBER: PCT/US05/13327



Certified by

Don W. Dudas

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EV496035557US

7513 U.S. P.T.D.

102104

[Page 1 of 2]

Date 10/21/2004

REGISTRATION NO. 45,260

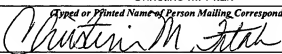
REGISTRATION NO. _____
(if appropriate)

Docket Number

TELEPHONE 989-496-3101

The collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10) Applicant(s): Shaow Burn Lin			Docket No. DC10102 PSP 1	
Application No.	Filing Date	Examiner	Customer No. 00137	Group Art Unit
Invention: Vesicles of High Molecular Weight Silicone Polyethers				
<p>I hereby certify that the following correspondence:</p> <div style="border: 1px solid black; height: 40px; margin: 10px 0;"></div> <p>Provisional Application, Cover Sheet and Return Postcard</p> <p style="text-align: center;"><i>(Identify type of correspondence)</i></p> <p>is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on</p> <p style="text-align: center;">21-Oct-04</p> <p style="text-align: center;"><i>(Date)</i></p> <div style="text-align: right; margin-top: 20px;"><p>Christine M. Fitak</p><hr/><p><i>(Typed or Printed Name of Person Mailing Correspondence)</i></p><p></p><hr/><p><i>(Signature of Person Mailing Correspondence)</i></p><p>EV496035557US</p><hr/><p><i>("Express Mail" Mailing Label Number)</i></p></div>				
<p style="text-align: center;">Note: Each paper must have its own certificate of mailing.</p>				

**UNITED STATES PATENT APPLICATION
FOR**

Vesicles of High Molecular Weight Silicone Polyethers

Having the inventor(s):

Shaow Burn Lin

FIELD OF THE INVENTION

This application relates to vesicle compositions from high molecular weight silicone polyethers, methods for preparing the vesicle compositions, and personal, household, and healthcare formulations containing the vesicle compositions.

BACKGROUND OF THE INVENTION

The aggregation behavior of surfactants in aqueous media is a robust area of investigation. Various vesicle compositions, such as liposomes and the like, have been developed for many applications with particular emphasis on the design of such systems for delivery of active materials via a pharmaceutical or personal care product formulation. Long-standing needs in this field are to identify vesicle compositions that form and entrap actives easily, are stable under various chemical and mechanical stresses, and yet are able to deliver the actives in a controlled manner under desired conditions. To this end, many classes and types of surfactants have been investigated for their ability to form vesicles and thus entrap and deliver actives.

Vesicles derived from silicone surfactants, and more particularly silicone polyether surfactants, are of interest because of additional inherent benefits that this class of surfactants possesses vs other types. For example, silicone surfactants often have improved aesthetics in personal care formulations.

The aggregation behavior of certain silicone polyethers has been discussed along with their ability to form vesicles. For example, US Patents 5,364,633 and 5,411,744 by Hill

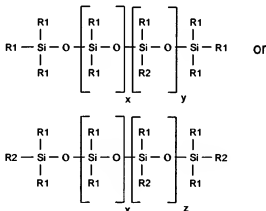
teaches the self-assembly of certain silicone polyethers in aqueous media to form vesicles. PCT Application US2003/38455 by Lin teaches the entrapment of various oils in certain silicone polyether vesicles and their use in various personal care formulations.

While these references represent advancements in the art, a need still exists to create
 5 silicone vesicles having improved stability. For example, the silicone vesicles formed from the self-assembly procedures can lack durability. This lack of durability can limit the processing conditions they can be subject to in the formation of various finished products. Furthermore, such self-assembled silicone vesicles can lack the ability to provide sustained release of loaded actives over an extended period of time. Thus, a need exists for a process to
 10 prepare silicone vesicles having improved durability and the ability to release loaded actives over an extended period of time.

The present inventors have discovered that high molecular weight silicone polyethers (SPEs) form vesicle compositions in aqueous media. The vesicle compositions possess enhanced stability and are useful to prepare formulations for the delivery of personal,
 15 household, and healthcare active materials.

SUMMARY OF THE INVENTION

The present invention relates to vesicle compositions comprising a silicone polyether having a structure represented by:



20

where R1 represents an alkyl group containing 1-6 carbon atoms;

R2 represents the group $-(\text{CH}_2)_a\text{O}(\text{C}_2\text{H}_4\text{O})_b(\text{C}_3\text{H}_6\text{O})_c\text{R}_3$;

x is 251-1,000; y is 1-500; z is 1-500; a is 3-6; b is 4-20; c is 0-5;

and R3 is hydrogen, a methyl group, or an acyl group.

The present invention further relates to a process for making a vesicle composition comprising;

I) mixing,

5 A) a silicone polyether copolymer, as described above,

B) an optional water miscible volatile solvent,

C) water,

to form an aqueous dispersion of the silicone polyether copolymer,

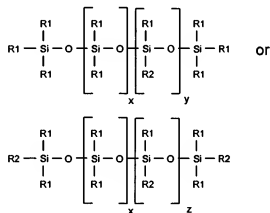
II) optionally, removing the water miscible volatile solvent from the aqueous

10 dispersion to form the vesicle composition.

Furthermore, the present invention relates to personal, household, and healthcare formulations containing the vesicle compositions.

DETAILED DESCRIPTION OF THE INVENTION

15 The vesicle compositions of the present invention comprise a silicone polyether having an average structure represented by:



In these structures, R1 represents an alkyl group containing 1-6 carbon atoms such as methyl, ethyl, propyl, butyl, pentyl, and hexyl; R2 represents the group -

20 $(\text{CH}_2)_a\text{O}(\text{C}_2\text{H}_4\text{O})_b(\text{C}_3\text{H}_6\text{O})_c\text{R}_3$; x has a value of 251-1,000, alternatively 251 - 750, or alternatively 251 - 500; y has a value of 1-500, alternatively 1- 100, or alternatively 2 - 50; z has a value of 1-500, or alternatively 1 - 100; m has a value of 3-5; n is one; a has a value of

3-6; b has a value of 4-20; c has a value of 0-5; and R3 is hydrogen, a methyl group, or an acyl group such as acetyl. Typically, R1 is methyl; b is 6-12; c is zero; and R3 is hydrogen.

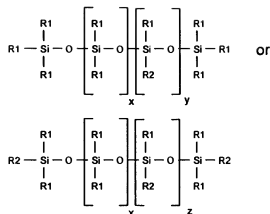
As used herein, "vesicle" is the common art term referring to entities formed from the aggregation of surfactant and/or lipid molecules in aqueous medium, characterized by the presence of one or more walls or membranes formed from a surfactant and/or lipid compound creating one or more internal voids. The walls or membranes formed by the surfactant and/or lipid in vesicles can be unilamellar, bilamellar, oligolamellar, or multilamellar structures. The formation of vesicles can be confirmed by techniques common in the state of the art. Typically, the lamellar phase structure in vesicles exhibit birefringence when examined with a cross polarizing microscope. Alternatively, the formation of vesicles can be demonstrated by Cyro-Transmission Electron Microscopy (Cryo-TEM) techniques.

The silicone polyethers useful to prepare the vesicle compositions of the present invention can be prepared by any method known in the art for preparing such copolymers. Typically however, the SPEs useful in the preparation of the vesicle compositions of the present invention are obtained by reacting an SiH containing organopolysiloxane with a polyoxyethylene having an unsaturated hydrocarbon group at a molecular terminal, in a hydrosilylation reaction. Typically, the molar ratio of the unsaturated hydrocarbon groups to SiH in the reaction is at least 1:1.

The vesicle compositions of the present invention can be prepared by mixing the SPEs with water using any technique known in the state of the art for creating vesicle compositions. The type and extent of the mixing technique will depend on the specific structure of the SPE chosen. Typically, the formation of vesicles from the SPEs of the present invention will require the presence of a water soluble solvent to facilitate the formation of vesicles. In a preferred embodiment, the vesicle compositions of the present invention are prepared using a process comprising;

I) mixing,

A) a silicone polyether having a structure represented by:



where R1 represents an alkyl group containing 1-6 carbon atoms;

R2 represents the group $-(\text{CH}_2)_a\text{O}(\text{C}_2\text{H}_4\text{O})_b(\text{C}_3\text{H}_6\text{O})_c\text{R}_3$;

x is 251-1,000; y is 1-500; z is 1-500; a is 3-6; b is 4-20; c is 0-5;

and R3 is hydrogen, a methyl group, or an acyl group,

B) a water miscible volatile solvent,

C) water,

to form an aqueous dispersion of the silicone polyether copolymer,

II) optionally, removing the water miscible volatile solvent from the aqueous

dispersion to form the vesicle composition.

The silicone polyether, component A), is the same as described above.

Component B) is a water-miscible volatile solvent. As used herein "water-miscible"

means the solvent forms a dispersion with water at room temperature for at least several

hours. "Volatile" means the solvent has a higher vapor pressure than water at various

temperatures. As such, when the aqueous dispersion of the organopolysiloxane and solvent are subjected to conditions to remove the solvent, such as heating the dispersion under reduced pressures, the solvent is primarily removed first, allowing all or most of the water to remain in the composition.

Suitable water-miscible volatile solvents for vesicle dispersion preparation include organic solvents such as alcohols, ethers, glycols, esters, acids, halogenated hydrocarbons, diols. The organic solvents should be miscible with water at the proportion and lower in order to effectively disperse silicones and maintain stable and uniform dispersion overtime. For the

purpose of illustration, water-miscible alcohols include methanol, ethanol, propanol, isopropanol, butanol, and higher hydrocarbon alcohols; ethers include glycol ethers, methyl-ethyl ether, methyl isobutyl ether (MIBK), etc; glycols include propylene glycols, esters include esters of triglycerol, the esterification products of acid and alcohol; halogenated hydrocarbons include chloroform. Typically water-miscible organic solvents are solvents with relatively low boiling points ($<100^{\circ}\text{C}$) or high evaporation rate, so they may be removed under vacuum with ease. The most preferred water-miscible organic solvents for this invention are volatile alcohols including methanol, ethanol, isopropanol, and propanol. These alcohols can be removed from aqueous mixtures containing silicone vesicle dispersions via vacuum stripping at ambient temperature.

The order of mixing components A), B), and C) is not critical, but typically A) and B) are first mixed and then water added to the mixture. There are no special requirements or conditions needed for effecting the mixing of components A), B), and C). The mixing can be conducted in a batch, semi-continuous, or continuous process.

The amount of components A), B), and C) can vary in the process, but typically range as follows;

A) 2 to 50 wt%, alternatively 2 to 25 wt %, or alternatively 2 to 15 wt%,

B) 0 to 50 wt%, alternatively 2 to 30 wt %, or alternatively 2 to 20 wt%,

C) sufficient amount to provide the sum of the wt% of A), B), and C) to equal 100%

The amount of B) water-miscible volatile solvent used to disperse the SPE depends on the type of organopolysiloxane and how much hydrophilic groups are present. Typically, the aqueous mixture to effectively disperse silicones comprises of 5 to 80 parts of solvent and 20 to 95 parts of water; alternatively 5 to 50 parts of water, or alternatively 10 to 40 parts water.

The formation of vesicles in the compositions of the present invention can be confirmed by techniques common in the state of the art. Typically, vesicles having a lamellar phase structure which exhibit birefringence when examined with a cross polarizing microscope. Alternatively, the formation of vesicles can be demonstrated by Cryo-Transmission Electron Microscopy (Cryo-TEM) techniques. Particle size measurements can also be used to indicate that the organopolysiloxanes are sufficiently dispersed in aqueous medium typical of vesicle sizes. For example, average particle sizes of less than $0.500\ \mu\text{m}$

(micrometers), are typical for dispersed vesicles. Vesicles having a average particle size of less than 0.200 μm , or 0.100 μm are possible with the teachings of the present invention.

The present invention also relates to vesicle compositions further comprising a personal, household, or health care ingredient. Thus, the vesicle compositions can be used to entrap, and subsequently deliver after application, a personal, household care, or health care ingredient. A listing of possible personal, household, or health care ingredients is taught in WO 03/101412, which is incorporated herein by reference. The personal or health care ingredient can also be selected from a personal or health care "active", that is, any compound known to have either cosmetic and/or pharmaceutical activity. A representative listing of such personal or health care actives are disclosed in US Patent 6,168,782, which is hereby incorporated by reference.

Compositions prepared according to the invention can be used in various over-the-counter (OTC) personal care compositions, health care compositions, and household care compositions, but especially in the personal care arena. Thus, they can be used in antiperspirants, deodorants, skin creams, skin care lotions, moisturizers, facial treatments such as acne or wrinkle removers, personal and facial cleansers, bath oils, perfumes, colognes, sachets, sunscreens, pre-shave and after-shave lotions, liquid soaps, shaving soaps, shaving lathers, hair shampoos, hair conditioners, hair sprays, mousses, permanents, depilatories, hair cuticle coats, make-ups, color cosmetics, foundations, blushes, lipsticks, lip balms, eyeliners, mascaras, oil removers, color cosmetic removers, nail polishes, and powders.

EXAMPLES

The following examples are presented to further illustrate the compositions and methods of this invention, but are not to be construed as limiting the invention. All parts and percentages in the examples are on a weight basis and all measurements were obtained at 23°C, unless indicated to the contrary.

Materials

Representative high molecular weight silicone polyethers, useful in the vesicle compositions of the present invention, were prepared by the hydrosilylation of high molecular weight methyl-hydrogen polysiloxanes (designated as MD_xD_yM in which x

designates the number of dimethyl siloxy units, and y the number of methyl-hydrogen siloxy units respectively) with a monoallyloxy polyoxyethylene having a M_n of 500 (AE501 Dow Chemical, Midland MI) using well known techniques.

- As used in the examples herein, SPE1 denotes the silicone polyether prepared from the reaction of MD₂₆₀D'₁₅M with AE501, and SPE2 the silicone polyether prepared from the reaction of MD₅₂₀D'₃₀M with AE501.

Testing Procedures

Particle Size

Cryo-Transmission Electron Microscopy (TEM)

- The vesicle compositions were analyzed via Cryo-TEM techniques according to the following procedure. Around 2.3 μ l of aqueous sample solution was loaded using a micropipette on a lacey carbon film coated Cu TEM grid that was cleaned and rinsed with acetone and chloroform. The samples were diluted to 5% solution with de-ionized water. The excess fluid on the grid surface was removed by blotting the surface with a filter paper for 1.5 second to make an aqueous thin film for TEM. The grid was then plunged into a liquid ethane contained in a small vessel located in a larger liquid nitrogen vessel under -175°C atmosphere in the cryo-plunge system to vitrify the water film on the grid and to avoid water crystallization. The quenched sample grid was transferred in to the cryo-grid box in the cryo-plunge system. The grid box containing the sample was transferred into a Gatan cryo-transfer system filled with liquid nitrogen and loaded in a cryo-TEM stage, which has been positioned in the cryo-transfer system and cooled down to below -160°C . The sample was loaded in TEM (JEOL 2000FX) and the images were observed at below -160°C . A much colder finger, cooled to -180°C in TEM using liquid nitrogen, was present to reduce any possible contamination on the cold specimen surface under high vacuum during TEM analysis. The digital images, as shown herein, were taken using a Gatan CCD camera attached at the bottom of the TEM column and Digital Micrograph software.

Example 1 - 3

A vesicle dispersion was successfully prepared by dispersing 44.3 g of SPE1 in a mixture of 73.77 g ethanol and 165.39 g water. A uniform dispersion with milky appearance was observed. The average particle size was 0.274 μm , as summarized in Table 1 as Example 1.

A uniform dispersion with even smaller particle size was made from SPE1 by further homogenizing through a high pressure, high shear unit like Microfluidizer, summarized in Table 1 as Example 2.

A stable dispersion of SPE1 with small particle size in largely water was prepared by further stripping off the volatile alcohol solvent. As shown by Example 3 in Table 1, the final dispersion has a composition of 20 % SPE vesicles, 5% alcohol and 75% water.

Table 1

Example	1	2	3
Dispersion type	Neat SPE	Neat SPE	Neat SPE
Mix Method	Mixed	Mixed, Microfluidized	Microfluidized, stripped
EtOH, g	73.770	73.770	26.49
SPE1 (MD ₂₆₀ D'15M), g	44.280	44.280	15.89
De-ionized water, g	165.39	165.39	59.37
Batch, before strip, g			101.75
Volatiles Removed, g			22.6
Final batch size, g	283.4	283.4	79.1
Wt. % SPE Polymer	15.62	15.62	20.09
Wt. % Alcohol	26.03	26.03	4.87
Wt. % Water	58.35	58.35	75.04
Appearance	Milky, uniform dispersion	Hazy to cloudy dispersion	Cloudy dispersion
Average particle, μm	0.274	0.0945	0.1011
D(v, 0.5), μm	0.2687	0.0830	0.0918
D(v, 0.9), μm	0.361	0.1539	0.1624
Peak 1, diameter, μm	0.2687	0.0830	0.0918
Peak 1, volume %	100%	100%	100%

Examples 4 – 6***Vitamin A palmitate entrapped in high DP SPE vesicle dispersion***

5

The following examples show vitamin A palmitate can be incorporated into high DP SPEs stable vesicles in water dispersions.

10 A uniform dispersion was prepared by mixing 9.74 g of vitamin A palmitate with 44.74 g of SPE1 and isopropanol and ethanol, as described in Table 2, Example 4. Water was incorporated and mechanically mixed to form a uniform dispersion. The final mixture was a yellowish dispersion with average particle size of 0.367 μm .

15 The vitamin A palmitate entrapped SPE dispersion can be further reduced in particle size by passing through a high pressure, high shear processor like Microfluidizer, as described by Example 5 in Table 2. The final dispersion was a smooth, yellowish dispersion with average particle size of about 0.137 μm .

20 The vitamin A palmitate entrapped SPE dispersion can be made stable in an aqueous mixture with minimal alcohol present. As illustrated in Table 2, the volatile alcohols in the formulation of Example 2 were stripped off under vacuum at ambient temperature. The final dispersion is summarized as Example 6 in Table 2. The dispersion was a smooth, uniform light yellowish dispersion with average particle size of 0.156 μm .

Table 2

Example #	4	5	6
Mix Method	Mixed	Mixed, MicroFluidized	Microfluidized, stripped
Vitamin A Palmitate, g	9.74	9.74	6.82
Isopropanol, g	9.74	9.74	6.86
EtOH, g	69.5	69.5	48.82
SPE1, g	44.74	44.74	31.42
De-ionized water, g	165.15	165.15	115.98
Batch, before strip, g			209.88
Volatiles Removed, g			55.2
Final batch size, g	298.86	298.86	154.7
Wt. % SPE Polymer	14.97	14.97	20.31
Wt. % VAP	3.25	3.25	4.41
Wt. % Alcohol	26.52	26.52	0.31
Wt. % Water	55.26	55.26	74.97
Appearance	Dull yellow dispersion	Pale yellow, smooth	Smooth milky yellow
Average particle, μm	0.367	0.1371	0.1557
D(v, 0.5), μm	0.353	0.1234	0.1426
D(v, 0.9), μm	0.514	0.2279	0.2349
Peak 1, diameter, μm	0.353	0.1234	0.1426
Peak 1, volume %	100%	100%	100%

Examples 7 - 10

- Two sets of vesicle dispersions were prepared for Cryo-TEM evaluations, following similar procedures as described in the examples above. The formulations for the vesicle dispersions are summarized in Tables 3 and 4. The Cryo-TEM images are shown in figures 1 and 2.

Table 3

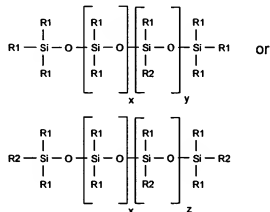
Example	7	8
Process History	As Made	Mixed, then stripped
MD ₂₆₀ D'15M SPE1, g	25.36	22.84
IPA, g	75.47	67.96
Water, g	150.22	135.27
Batch size before strip, g	251.05	226.06
Volatile removed, g		68.05
Batch size after strip, g		158.01
Vesicle dispersion composition		
% SPE	10.1	14.5
% Alcohol	30.1	0.0
% Water	59.8	85.5
Dispersion appearance	water-white clear	milky dispersion
Average particle size Mv, μm	0.0314	0.591
D(v, 0.5), μm	0.02977	0.508
D(v, 0.9), μm	0.044	1.078

Table 4

Example	9	10
Process History	Mixed	Mixed, then stripped
MD ₅₂₀ D'30M (SPE2), g	25.28	22.88
IPA, g	75.28	68.12
Water, g	150.15	135.87
Batch size before strip, g	250.71	226.86
Volatile removed, g		69.31
Batch size after strip, g		157.55
Vesicle dispersion composition		
Wt. % SPE	10.1	14.5
Wt. % Alcohol	30.0	0.0
Wt. % Water	59.9	85.5
Dispersion appearance	Water-white clear	Milky dispersion
Average particle size Mv, μm	0.0372	0.973
D(v, 0.5), μm	0.02532	0.672
D(v, 0.9), μm	0.0376	2.116

CLAIMS

1. A vesicle composition comprising a silicone polyether having a structure represented by:



where R1 represents an alkyl group containing 1-6 carbon atoms;

R2 represents the group $-(\text{CH}_2)_a\text{O}(\text{C}_2\text{H}_4\text{O})_b(\text{C}_3\text{H}_6\text{O})_c\text{R}_3$;

x is 251-1,000; y is 1-500; z is 1-500; a is 3-6; b is 4-20; c is 0-5;

and R3 is hydrogen, a methyl group, or an acyl group.

2. The vesicle composition of claim 1 wherein x ranges from 251 to 750.

3. A process for making a vesicle composition comprising;

I) mixing,

A) the silicone polyether copolymer of claim 1,

B) an optional water miscible volatile solvent,

C) water,

to form an aqueous dispersion of the silicone polyether copolymer,

II) optionally, removing the water miscible volatile solvent from the aqueous

dispersion to form the vesicle composition.

4. The vesicle composition produced by the process of claim 3.

5. The vesicle composition of claim 1 or 4 further comprising a personal, household, or healthcare active ingredient.

6. A personal, household, and healthcare composition comprising the vesicle composition of
5 claims 1, 4 or 5.

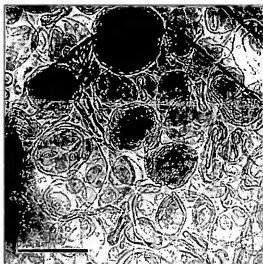
ABSTRACT

Vesicle compositions from high molecular weight silicone polyether copolymers, methods for preparing the vesicle compositions, and personal, household, and healthcare

5 formulations containing the vesicle compositions are disclosed.

Figure 1

A Cryo-TEM image of the vesicle dispersion prepared for Example 8 from MD₂₆₀D⁺15M High DP (SPE1).



BEST AVAILABLE COPY

Figure 2

A Cryo-TEM image of the vesicle dispersion prepared for Example 10
from MD₅₂₀D'30M High DP (SPE2).



BEST AVAILABLE COPY